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3000 7590 06/08/2009 CAESAR, RIVISE, BERNSTEIN, COHEN & POKOTILOV, LTD. 11TH FLOOR, SEVEN PENN CENTER 1635 MARKET STREET PHILADELPHIA, PA 19103-2212				
EXAMINER				
RIPA, BRYAN D				
ART UNIT		PAPER NUMBER		
1795				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

# Office Action Summary

## Application No.

10/597,696

## Applicant(s)

SCHNELLE ET AL.

## Examiner

BRYAN D. RIPA

## Art Unit

1795

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 30-58 is/are pending in the application.
- 4a) Of the above claim(s) 50-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-36; 38-49 is/are rejected.
- 7) ☒ Claim(s) 37 is/are objected to.
- 8) ☒ Claim(s) 30-58 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 03 August 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SI/08)  
Paper No(s)/Mail Date 8/3/06; 1/31/07
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 30-49, drawn to a microfluidic system.

Group II, claim(s) 50-58, drawn to a method of using the microfluidic system.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. Each of the inventions recites the use of a microfluidic system as in present claim 30. This subject matter was determined to lack inventive step in the international search report of 2/6/05, citing WO 03/066191. Accordingly, the inventions lack a common special technical feature that makes a contribution over the art.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product

are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

During a telephone conversation with David Tener on May 18, 2009 a provisional election was made without traverse to prosecute the invention of group 1, claims 30-49. Affirmation of this election must be made by applicant in replying to this Office action. Claims 50-58 are withdrawn from further consideration by the examiner, see 37 CFR 1.142(b), as being drawn to a non-elected invention.

### ***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 33, 44 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 33, claim 33 recites the limitation of "an area of the first carrier flow" and "an area of the second carrier flow." However, the carrier flow comprises a moving fluid and consequently any such area of the carrier flow would not be stationary. As a result, it is unclear where the first and second measuring stations are to be placed based on the claim language as presently written.

Regarding claims 44 and 45, claim 44 recites the limitation "the field cage" in the second line. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 30 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Oakey et al., (WIPO Pub. No. 2003/066191A1) (hereinafter referred to as "OAKEY").

Regarding claim 30, OAKEY teaches a microfluidic system comprising a first carrier flow supply line (see page 3 lines 4-6) capable of supplying a first carrier flow with particles suspended therein; a first carrier flow output line (see page 3 lines 4-6) capable of withdrawing at least a part of the first carrier flow with the particles suspended therein; a second carrier flow supply line (see page 3 lines 4-6) capable of supplying a second carrier flow with particles suspended therein; and a process chamber, i.e. a microfluidic flow channel, wherein the first and second carrier flow supply lines open into the process chamber and the first carrier flow output line is discharged out of the process chamber (see page 3 lines 4-13), capable of use for examining, observing, manipulating and/or selecting the particles. See also figures 6 and 14 with accompanying discussion.

Please note, the examiner is interpreting the limitations "for supplying ...", "for withdrawing ...", and "for examining ..." to be statements of intended use. See MPEP §

2114. As a result, the prior art structure must just be capable of functioning in that manner in order to meet the claim limitations.

Regarding claim 42, OAKLEY teaches the microfluidic system wherein at least one second carrier flow output line is discharged from the process chamber (see page 3 lines 4-6).

3. Claims 30-36, 40, 41 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Muller et al., (U.S. Pat. No. 6,492,175) (hereinafter referred to as "MULLER").

Regarding claim 30, MULLER teaches a microfluidic system comprising a first carrier flow supply line (see channel 71) capable of supplying a first carrier flow with particles suspended therein; a first carrier flow output line (see output channel on the right-hand side of figure 7) capable of withdrawing at least a part of the first carrier flow with the particles suspended therein; a second carrier flow supply line (see channel 72) capable of supplying a second carrier flow with particles suspended therein; and a process chamber (see regions A and B), wherein the first and second carrier flow supply lines open into the process chamber and the first carrier flow output line is discharged out of the process chamber (see channels 71 and 72 opening into the process chamber at region A and the first carrier flow output line being discharged out of the process chamber to the right of region B), capable of use for examining,





Please note, similar to the claim interpretation of claim 30 discussed above, the examiner is interpreting the claim limitations “for examining ...” of each carrier flow stream to be statements of intended use. See MPEP § 2114. As a result, the prior art structure must just be capable of functioning in that manner in order to meet the claim limitations.

Regarding claim 32, MULLER teaches the microfluidic system wherein the first carrier flow and the second carrier flow run adjacent to one another in the process chamber at in an examination area located upstream (see figure 7 above showing the channels 71 and 72 with there respective fluid streams running adjacent to one another in the process chamber). See figure 7 above.

Regarding claim 33, MULLER teaches the microfluidic system wherein the first measuring station is arranged in an examination area of the process chamber in an area of the first carrier flow whereas the second measuring station is arranged in the examination area of the process in an area of the second carrier flow and adjacent to the first measuring station as regards a direction of flow (see figure 7 above showing detectors 78 in the process chamber and adjacent to each other with respective to the direction of the fluid flows). See figure 7 above.

Regarding claim 34, MULLER teaches the microfluidic system wherein a dividing wall is arranged in the examination area of the process chamber between the first

carrier flow and second carrier flow, the dividing wall being impermeable for the particles and/or for the carrier flows (see second spacer in figure 7 above which is impermeable to the large cells 74 and small cells 75). See figure 7 above.

Regarding claim 35, MULLER teaches the microfluidic system wherein a dielectrophoretic field cage is arranged in the process chamber in order to fix the particles (see col. 8 lines 19-25 and col. 5 lines 40-49 teaching the electrode configuration consisting of a three-dimensional electrode arrangement which is used to hold or fix the particles). See figure 7 above.

Regarding claim 36, MULLER teaches the microfluidic system wherein the field cage is arranged downstream behind the first measuring station and the second measuring station (see electrodes 77 and 77a being downstream from detectors 78). See figure 7 above.

Regarding claim 40, MULLER teaches the microfluidic system wherein at least one centering unit that holds that centers the particles is arranged in the process chamber (see portion of spacer above that acts to center the small cells 75 in region B). See figure 7 above.

Regarding claim 41, MULLER teaches the microfluidic system wherein at least one holding unit that holds the particles is arranged in the process chamber (see

electrodes 77 and col. 5 lines 29-49 discussing the operation of the electrodes used for electroporation having to hold the particles). See figure 7 above.

Regarding claim 49, MULLER teaches a cell sorter comprising the microfluidic system (see figure 7 above acting to sort the large cells 74 from the small cells 75). See figure 7 above.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over MULLER.

Regarding claim 38, MULLER teaches a selection unit arranged in the direction of flow before the measuring stations and the field cage, not between, that selects certain particles from the first carrier flow supply lines to send to the field cage.

However, the placement of the selection unit between the measuring stations and the field cage is an obvious rearrangement of parts. Moreover, one of ordinary skill in the art would be motivated to have the selection unit after the measuring stations in order to facilitate selection based on some measured aspect of the particle or cell.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to rearrange the order of the selection unit and measuring stations or MULLER in order to obtain a microfluidic system as claimed.

5. Claims 39 and 42- 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over MULLER and in view of Muller et al., "A 3-D Microelectrode System For Handling and Caging Single Cells and Particles" *Biosensors & Bioelectronics* 14, pages 247-256 (1999) (hereinafter referred to as "MULLER II") with evidence from OAKLEY.

Regarding claim 39, MULLER does not teach the microfluidic system further comprising a third measuring station for examining the particles fixed in the field cage.

However, MULLER II teaches a measuring station for examining the particles fixed in a field cage (see page 248 teaching the trapping of the cells in the field cage to allow sufficient time for analysis).

Consequently, as shown by MULLER II, a person of ordinary skill in the art would accordingly have recognized the placing of an additional measuring station over the field cage to facilitate the examination of the particles fixed in the field cage.

Applying a known technique to a known device (method or product) ready for improvement to yield predictable results is likely to be obvious. See *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395-97 (2007) (see MPEP § 2143, D.).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to add a third measuring station to the microfluidic system of MULLER as shown by MULLER II in order to obtain the predictable result of having a measuring station for examining the particles fixed in the field cage.

Regarding claim 42, MULLER is silent as to the details of the carrier flow output lines. More specifically, MULLER does not explicitly teach the microfluidic system wherein at least one second carrier flow output line is discharged from the process chamber.

However, MULLER II teaches there being at least one second carrier flow output line which is discharged from the process chamber to allow for the separation of the particles or cells into separate fractions (see pages 248 and 255 and figure 5b). Moreover, MULLER teaches the possibility of adding additional channels (see col. 8 lines 29-32).

Consequently, as shown by MULLER II, a person of ordinary skill in the art would accordingly have recognized the use of having multiple output channels in order to facilitate the separation of the cells into different fractions.

The combination of familiar elements is likely to be obvious when it does no more than yield predictable results. See *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395-97 (2007) (see MPEP § 2143, A.).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the output channels of MULLER II with the microfluidic system of MULLER to obtain the predictable result of having a second carrier flow output line as claimed.

Regarding claim 43, MULLER does not teach the microfluidic system wherein a sorting unit is arranged in a downstream area of the process chamber that sorts the particles into a carrier flow output line.

However, MULLER II teaches the use of a sorting unit to sort particles according to a set of specified parameters into a particular carrier flow output line (see page 248 and 255 teaching the use of a switch or sorting unit to separate the sample into separate fractions).

Consequently, as shown by MULLER II, a person of ordinary skill in the art would accordingly have recognized the use of a sorting unit after the particles leave the process chamber of MULLER to separate the particles into separate carrier flow output lines.

The combination of familiar elements is likely to be obvious when it does no more than yield predictable results. See *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395–97 (2007) (see MPEP § 2143, A.).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the sorting unit of MULLER II after the microfluidic system of MULLER in order to obtain the predictable result of having a sorting unit arranged in a downstream area of the process chamber as claimed.

Regarding claim 44, MULLER as modified by MULLER II teaches the second carrier flow output line discharged behind the field cage from the process chamber in a laterally offset manner (see figure 7 from MULLER above showing electrodes 77 and



77a within the process chamber and upstream from any carrier flow output lines; see also figure 5b from MULLER II showing the two carrier flow output lines being discharged from the process chamber in a laterally offset manner).

Regarding claim 45, as mentioned previously MULLER is silent as to the details of the carrier flow output lines. However, MULLER II teaches there being two output lines laterally offset from the process chamber (see page 255 and figure 5b). Moreover, as evidenced by OAKLEY, it was well known in the art that depending on the application the microfluidic system might have a need for more than one or two output lines (see figure 8 and page 14 lines 3-15). See also the rejection of claim 35 above.

The mere duplication of parts, without any new or unexpected results, is within the ambit of one of ordinary skill in the art. See *In re Harza*, 124 USPQ 378 (CCPA 1960) (see MPEP § 2144.04).

Therefore it would have been obvious to one of ordinary skill in the art at the time of invention to add an additional carrier flow output line that is discharged from the process chamber in a laterally offset manner after the field cage.

Regarding claim 46, MULLER teaches the microfluidic system further comprising at least one centering unit that centers the particles and is arranged in the process chamber (see deflection electrodes 76 which act to direct the particles into the center their respective channels), at least one holding unit that holds the particles and is arranged in the process chamber (see electrodes 77 and 77a and discussion above

with respect to claim 35 as to how those electrodes act as a dielectrophoretic holding unit), wherein the centering unit and the holding unit have a dielectrophoretic electrode arrangement (see figure 7).

MULLER does not teach a selection unit comprising a dielectrophoretic electrode arrangement arranged in the direction of flow between the measuring stations and the field cage that selects certain particles from the first carrier flow supply line and supplies them to the field cage.

However, as discussed above in relation to claim 38, such a limitation would have been obvious to one of ordinary skill in the art at the time of invention.

Also, MULLER does not teach a sorting unit comprising a dielectrophoretic electrode arrangement arranged in a downstream area of the process chamber that sorts the particles into the first carrier flow output line or second carrier flow output line.

However, as discussed above in relation to claim 43, such a limitation would have been obvious to one of ordinary skill in the art at the time of invention.

Therefore, it would have been obvious to one of ordinary skill in the art to alter the microfluidic system of MULLER in order to obtain a microfluidic system as claimed.

Regarding claim 47, MULLER does not explicitly teach the microfluidic system wherein a holding unit is arranged in at least one of the carrier flow output lines in order to intermediately store the particles in the output line.

However, MULLER II does teach the use of a dielectrophoretic cage or holding unit (see page 254). Moreover, one of ordinary skill in the art would have recognized

the use of a field cage or some similar electrode configuration to collect or hold particles dielectrically.

In addition, MULLER teaches the option of dielectrically collecting the particles after the particles have passed through the microfluidic system of figure 7 (see col. 8 lines 26-28).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to include the field cage of MULLER II after the microfluidic system of MULLER in order to facilitate the collection of the particles.

5. Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over MULLER in view of Orwar et al., (U.S. Pub. No. 2003/0104588) (hereinafter referred to as "ORWAR").

Regarding claim 48, MULLER does not explicitly teach the microfluidic system being a cell fusioner, i.e. having sufficient structure so as to be capable of fusing cells. MULLER, however, does disclose the device being used in conjunction with a cell fusioner (see col. 8 lines 26-28).

Moreover, ORWAR teaches an apparatus for use in a microfluidic system for fusing cells (see ¶43-48).

Therefore, it would have been appreciated by one of ordinary skill in the art to incorporate the cell fusioner of ORWAR with the microfluidic system of MULLER to

obtain the predictable result of having a cell fusioner comprising the microfluidic system as claimed.

***Allowable Subject Matter***

Claim 37 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter:

Regarding claim 37, the cited prior art neither teaches nor fairly suggests the field cage of MULLER being arranged in the process chamber substantially in the middle of the channel between the two carrier flows.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRYAN D. RIPA whose telephone number is 571-270-7875. The examiner can normally be reached on Monday to Friday, 9:00 AM to 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alexa Neckel can be reached on 571-272-1446. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/B. D. R./  
Examiner, Art Unit 1795

/Brian J. Sines/  
Supervisory Patent Examiner, Art Unit 1795